

(e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209490,
wherein said isolated nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor.

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53. (Amended) The isolated nucleic acid of Claim 52, wherein said hybridization occurs under high stringency conditions.

REMARKS

The foregoing amendments in the specification and claims are of formal nature and do not introduce new matter.

Prior to entry of the present amendments, claims 39-58 were pending in this application, and stood rejected on various grounds. The present Amendment and Response is accompanied by the payment of the requisite fee for a two-month extension of time, therefore, the present response is timely filed.

Specification

The specification was amended to reflect the current address of ATCC and to correct a minor typographical error.

Claim Rejections - 35 USC § 112, Second Paragraph

Claims 39-44, 47, 48, 52, 53 and dependent claims 45, 46, 49-51 and 55-58 were rejected as "being indefinite" in their reference to the extracellular domain of PRO339, which is a secreted polypeptide. Since the claims no longer refer to an extracellular domain, the current amendments believed to overcome this rejection.

Claims 52, 53 were rejected as "indefinite" in their reference to hybridization. As amended, Claim 52 recites moderately stringent conditions, and Claim 53 recites high stringency conditions. As noted by the Examiner, these stringency conditions are disclosed in the specification. In particular, moderately stringent conditions and high stringency conditions are defined, for example, at page 74, lines 4 *et seq.* Accordingly, Applicants respectfully submit that the rejections to Claims 52 and 53 under 35 U.S.C. § 112, second paragraph are overcome.

Claim Rejections - 35 USC § 101

Claims 39-58 were rejected under 35 USC § 101, since "the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility."

Claims 47 and 48 have been canceled. The rejection of the remaining claims is respectfully traversed.

Utility – Legal Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic

quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility.” In explaining the “substantial utility” standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase “immediate benefit to the public” or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be “currently available” to the public in order to satisfy the utility requirement. **“Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient,** at least with regard to defining a “substantial” utility.” (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P., 2107 II (B) (1) gives the following instruction to patent examiners: “If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility.”

Finally, the Utility Guidelines restate the Patent Office’s long established position that any asserted utility has to be “credible.” “Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant’s assertions.” (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Proper Application of the Legal Standard

Applicants submit that the gene amplification data provided in the present application are sufficient to establish a specific, substantial and credible utility for the PRO339 polypeptide coded for by the claimed nucleic acids.

Gene amplification is an essential mechanism for oncogene activation. It is well known that gene amplification occurs in most solid tumors, and generally is associated with poor prognosis. As described in Example 92 of the present application, the inventors isolated genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 8 (pages 230-234 of the specification), including primary lung cancers and colon cancers of the type and stage indicated in Table 8 (page 227). As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control (page 222, lines 34-36). Gene amplification was monitored using real-time quantitative TaqMan™ PCR. The gene amplification results are set forth in Table 9. As explained in the passage bridging pages 222 and 223, the results of TaqMan™ PCR are reported in ΔCt units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification, relative to control, two units correspond to 4-fold, 3 units to 8-fold, etc. amplification. PRO339 showed 2-3 fold gene amplification in a number of lung and colon tumors.

In assessing the value of these data, the Examiner notes that: "There is no specific information on what type of the normal tissue was used as a control and how many normals there were. A single normal sample is not sufficient for basing relative levels of many other samples." The Examiner has apparently overlooked that, as discussed above, control DNA was pooled from the cells of ten normal healthy individuals (page 222, lines 34-36). Accordingly, the results are not based on a single normal sample. The samples were obtained from blood cells as it is usual in similar gene amplification assays.

The attached Declaration by Audrey Goddard clearly establishes that the TaqMan™ real-time PCR method described in Example 92 has gained wide recognition for its versatility, sensitivity and accuracy, and is in extensive use for the study of gene

amplification. The facts disclosed in the Declaration also confirm that based upon the gene amplification results set forth in Table 9 one of ordinary skill would find it credible that PRO339 is a diagnostic marker of human lung and colon cancer. It is, of course, true that further research would be needed to develop PRO339 into a diagnostic product. Such follow-up tests could include the mapping of the PRO339 gene to a chromosome, which could be followed, for example, by dual-color FISH with DNA probes complementary to the PRO339 gene and the centromere of the chromosome to distinguish a locus-specific gene amplification from chromosome aneuploidy. However, the fact that such follow-up tests might be necessary, cannot properly lead to the legal conclusion that PRO339 lacks patentable utility.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. The attached Declaration by Audrey Goddard establishes that the asserted utility is viewed to be "credible" by one skilled in the art. Indeed, the logic underlying Applicants' assertion that PRO339 is a diagnostic marker of lung and colon cancer cannot be viewed as "seriously flawed," and the facts upon which the assertion is based are not inconsistent with the logic underlying the assertion. It is always possible that an invention fails on its way of development to a commercial product. Thus, despite recent advances in rational drug design, a large percentage of drug candidates fail, and never make it into a drug product. However, the USPTO is not the FDA, the law does not require that a product (drug or diagnostic) be currently available to the public in order to satisfy the utility requirement.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections under 35 U.S.C. 112, first paragraph

(a) Claims 39-58 were rejected under 35 USC § 112, first paragraph "since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention."

In response to the previous rejection under 35 U.S.C. 101, Applicants have shown that the specification discloses a substantial, specific and credible utility for the PRO339 polypeptide coded for by the claimed nucleic acids. This specific utility is now recited in the rejected claims. The Examiner has named no particular reasons why the specification would not be enabling for the use now recited in the claims. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of all pending claims on this ground.

(b) Claims 39-43, and 52-58 were also rejected under 35 USC § 112, first paragraph, for alleged lack of sufficient written description. The Examiner noted that the claims reciting various degrees of sequence identity with the sequence specifically disclosed or to a nucleic acid that hybridizes to SEQ ID NO:338 did not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature.

The claims as currently amended recite that the polypeptides coded for by the claimed nucleic acids are associated with the formation or growth of lung or colon tumor. This biological activity, coupled with a well defined, and relatively high degree of sequence identity is believed to sufficiently define the claimed genus, such that one skilled in the art at the effective priority date of the present application would be

reasonably accepted that the inventors were in the possession of the invention as claimed. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

35 USC §§ 102 and 103

Claims 39-44, 47, 49 and 52-58 were rejected under 35 USC 102(b) as "being anticipated by GenBank Accession No. AB037823 as evidenced by Strategene Cloning Systems catalog (1994)." In addition, claims 46 and 48 were rejected under 35 USC § 103(a) as allegedly obvious over GenBank Accession No. AB037823 and "Applicants' Admission on p.34, lines 5-6 and Fleming et al. (Dev., 124:2873-81 (1997))."

According to the Office Action, the effective date of the primary reference (GenBank Accession No. AB037823) is March 14, 2000. The gene amplification data, which support the utility of the polypeptides claimed in the present application were first disclosed in PCT/US00/03565 filed on February 11, 2000, the priority of which is claimed in the present application. Since the present application is entitled to at least the February 11, 2000 priority, GenBank Accession No. AB037823 is not prior art. Accordingly, the present rejections should be withdrawn.

Claims 52-54 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by US Patent 5,695,995, the Examiner stating that "US Patent 5,695,995 teach a nucleic acid of SEQ ID NO:16 that would hybridize to SEQ ID NO:338 of the instant application and is at least 10 nucleotides in length."

Anticipation under 35 U.S.C. § 102 requires that "every element of the claimed invention be identically shown in a single reference." (*In re Bond*, 910 F.2d 831,832 (Fed. Cir. 1990). Claims 52-54 recite an isolated nucleic acid that hybridizes under at

least moderately stringent conditions to a nucleic acid sequence encoding the polypeptide having the sequence SEQ ID NO: 339, wherein the nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor. However, the nucleic acid of US Patent 5,695,995 cited by the Examiner is not associated with the formation or growth of lung or colon tumor, nor would it be expected to hybridize under at least moderately stringent conditions to a nucleic acid sequence encoding the polypeptide having the sequence SEQ ID NO: 339, wherein the nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor. Accordingly, since the nucleic acid of US Patent 5,695,995 cited by the Examiner does not disclose at least these elements of claims 52-54, Applicants respectfully submit that US Patent 5,695,995 does not anticipate claims 52-54 and that the rejections of claims 52-54 are overcome.

Applicants note the citation of additional art, which was not relied upon in any of the rejections. Since the present application is entitled to the February 11, 2000 priority, WO2001153312 is not prior art. Similarly, none of the other references are believed to anticipate or render obvious any of the claims pending.

Attached hereto is a marked-up copy of the amendments made in the specification and claims. The attached sheets are entitled "Version with Markings to Show Changes Made."

All claims are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for extension of time, or credit overpayment to Deposit Account No. 08-1641.

Respectfully submitted,

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Version with Markings to Show Changes Made

In the Specification:

Replace the paragraph beginning at page 202, line 36 with the following amended paragraph:

A variety of protocols for measuring soluble or membrane-bound [PRo317] PRO317, using either polyclonal or monoclonal antibodies specific for that PRO317, are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), radioreceptor assay (RRA), and fluorescent activated cell sorting (FACS). A two-site monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on PRO317 is preferred, but a competitive binding assay may be employed. These assays are described, among other places, in Maddox *et al.* J Exp. Med., 158:1211 (1983).

Replace the paragraph beginning at page 250, line 1 with the following amended paragraph:

-- The following materials have been deposited with the American Type Culture Collection, [12301 Parklawn Drive, Rockville, MD], 10801 University Boulevard, Manassas, VA 20110-2209, USA (ATCC):--

In the Claims:

Claims 47 and 48 have been canceled.

Claims 39, 40, 41, 42, 43, 44 and 52 have been amended as follows:

39. (Amended) An isolated nucleic acid having at least 80% nucleic acid sequence identity to:

- (a) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339);
- (b) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;
- [(c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339);
- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;]
- [(e)](c) the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338);
- [(f)](d) the full-length coding sequence of the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338); or
- [(g)](e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209490,

wherein said isolated nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor.

40. (Amended) The isolated nucleic acid of Claim 39 having at least 85% nucleic acid sequence identity to:

- (a) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339);
- (b) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;
- [(c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339);
- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;]
- [(e)](c) the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338);

[(f)](d) the full-length coding sequence of the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338); or

[(g)](e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209490,

wherein said isolated nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor.

41. (Amended) The isolated nucleic acid of Claim 39 having at least 90% nucleic acid sequence identity to:

(a) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339);

(b) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;

[(c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339);

(d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;]

[(e)](c) the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338);

[(f)](d) the full-length coding sequence of the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338); or

[(g)](e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209490,

wherein said isolated nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor.

42. (Amended) The isolated nucleic acid of Claim 39 having at least 95% nucleic acid sequence identity to:

- (a) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339);
- (b) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;
- [(c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339);
- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;]
- [(e)][(c) the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338);
- [(f)][(d) the full-length coding sequence of the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338); or
- [(g)][(e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209490,

wherein said isolated nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor.

43. (Amended) The isolated nucleic acid of Claim 39 having at least 99% nucleic acid sequence identity to:

- (a) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339);
- (b) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;
- [(c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339);
- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;]
- [(e)][(c) the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338);

[(f)](d) the full-length coding sequence of the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338); or

[(g)](e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209490,

wherein said isolated nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor.

44. (Amended) An isolated nucleic acid comprising:

(a) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339);

(b) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;

[(c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339);

(d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;]

[(e)](c) the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338);

[(f)](d) the full-length coding sequence of the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338); or

[(g)](e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209490,

wherein said isolated nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor.

52. (Amended) An isolated nucleic acid that hybridizes under moderately stringent conditions to:

(a) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339);

- (b) a nucleic acid sequence encoding the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;
- [(c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339);
- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in Figure 118 (SEQ ID NO: 339), lacking its associated signal peptide;]
- [(e)](c) the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338);
- [(f)](d) the full-length coding sequence of the nucleic acid sequence shown in Figure 117 (SEQ ID NO:338); or
- [(g)](e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209490,

wherein said isolated nucleic acid encodes a polypeptide associated with the formation or growth of lung or colon tumor.

53. (Amended) The isolated nucleic acid of Claim 52, wherein said hybridization occurs under [stringent] high stringency conditions.

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